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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/791,951	03/03/2004	Kurt Friedrich Brandstadt	DOG 0084 PA	1997
23368 7590 01/09/2008 DINSMORE & SHOHL LLP ONE DAYTON CENTRE, ONE SOUTH MAIN STREET SUITE 1300 DAYTON, OH 45402-2023			EXAMINER PROUTY, REBECCA E	
			ART UNIT 1652	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

10/791,951

Applicant(s)

BRANDSTADT ET AL.

Examiner

Rebecca E. Prouty

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 October 2007 and 19 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 5-10, 12-14, 16, 19, 21, 22, 24, 25 and 27-35 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 5-10, 12-14, 16, 19, 21, 22, 24, 25, 27-35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

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A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on 10/11/07 and 10/19/07 have been entered.

Claims 2-4, 11, 15, 17, 18, 20, 23, and 26 have been canceled. Claims 1, 5-10, 12-14, 16, 19, 21, 22, 24, 25, 27-32 and newly presented claims 33-35 are still at issue and are present for examination.

Applicants' arguments filed on 10/11/07, have been fully considered and are not deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claims 33 and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s),

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at the time the application was filed, had possession of the claimed invention.

These claims recite the use of a group of organic reactants including specifically dimethyldiethoxygermane. However, the specification includes no support for the recitation of this specific organic reactant. Applicants state in their response that support for these claims can be found in the examples. However none of the examples of the instant specification recite use of any germanium compounds. As such this recitation is new matter.

Claims 1, 5-10, 12-14, 16, 21, 22, 24, 25, and 27-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of forming an organic siloxane by hydrolysis and condensation of an organic silane selected from trimethylethoxysilane,  $(\text{Me}_3\text{SiO}(\text{CH}_2\text{CH}_2\text{O})_4\text{CH}_3)$ , 3-glycidopropyldimethylethoxysilane, 1,1-dimethyl-1-sila-2-oxacyclohexane, and methyltriethoxysilane with trypsin or by condensation of the corresponding organic silanols with trypsin, does not reasonably provide enablement for forming any organic compound by reacting any organic reactant or organic intermediate reactant as defined in claims 16, 31, and 32 with any hydrolase selected from *Candida antarctica* lipase, *Candida antarctica* lipase B, *Rhizomucor miehei* lipase, wheat germ

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lipase, trypsin, cutinase papain, pepsin or a combination thereof or for any organic compound by reacting any organic reactant or organic intermediate reactant as defined in claim 1, with any hydrolase selected from trypsin and cutinase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 5-10, and 12-14 are so broad as to include forming any organic compound by reacting any organic reactant as defined in claim 1 (i.e., an enormous variety of silicon or germanium containing compounds) with any trypsin or cutinase. Claims 16, 21, 22, 24, 25, and 27-32 are so broad as to include forming any organic compound by reacting any organic reactant as defined in claims 16, 31, and 32 (i.e., 9 specific silicon or germanium containing compounds in claims 16, 21, 22, 24, 25, and 27-31 or the corresponding silanols in claim 32 with a hydrolase selected from *Candida antarctica* lipase, *Candida antarctica* lipase B, *Rhizomucor miehei* lipase, wheat germ lipase, trypsin, cutinase papain, pepsin. The claims are not commensurate in scope with the enabled invention with regard to the scope of organic reactants (or intermediate reactants) used, the scope of organic compounds formed, nor the scope of enzymes utilized as

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catalyst. The specification provides evidence that most hydrolase enzymes tested did not catalyze the hydrolysis or condensation of any organic silane at all, despite testing several different enzymes (see particularly examples 2 and 3). Furthermore, not only did most hydrolases tested not catalyze the instant reactions, there is clearly no unifying characteristics present in the few that were successful that could be used for the selection of other suitable enzymes from the enormous number of known hydrolases (or even known proteases). In fact even different sources of trypsin had distinctly different abilities to catalyze the claimed reactions. Furthermore, the specification provides substantial evidence that trypsin will not catalyze the hydrolysis and/or condensation of most of the enormous number of organic silanes or corresponding silanols included in the scope of the claims showing successful reactions with only trimethylethoxysilane,  $(\text{Me}_3\text{SiO}(\text{CH}_2\text{CH}_2\text{O})_4\text{CH}_3)$ , 3-glycidopropyldimethylethoxysilane, 1,1-dimethyl-1-sila-2-oxacyclohexane, and methyltriethoxysilane and provides absolutely no evidence that any corresponding germanium containing compounds can be used. The group of successful reactants do not share any unifying characteristics with which a skilled artisan could reasonably predict what other organic silanes or corresponding silanols could be used. As there are

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virtually an enormous number of possible combinations of enzymes and organic reactants encompassed in the claims, the specification shows that the vast majority of combinations are unsuccessful, and the specification provides absolutely no guidance for the selection of others combinations which are successful, it would require undue experimentation to practice the full scope of claimed methods.

Applicants argue that the specification provides several examples of monofunctional and polyfunctional organic reactants that may be contacted with hydrolase enzymes to catalyze the formation of organic molecules and organic intermediates which range in scope for both the breadth of the organic reactant and the hydrolase enzyme, and Applicants have taken that disclosure and defined the genera of organic reactants/intermediates and hydrolase enzymes accordingly. However this is simply an untrue statement. It is noted that for the scope of hydrolase enzymes recited in claims 16, 31, and 32 the specification has shown only one successful reaction for all of *Candida antarctica* lipase, *Candida antarctica* lipase B, *Rhizomucor miehei* lipase, wheat germ lipase, papain, and hog stomach pepsin (in which pepsin and papain reacted extremely poorly), not a single successful reaction using any cutinase and the one disclosed successful reaction used an organic reactant (i.e.,

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trimethylsilanol) not even recited in these claims. The results with trypsin in the examples in the specification make it abundantly clear that one success with one organic reactant is absolutely not predictive of success with other different organic reactants. Furthermore, it should be noted that each of trypsin, pepsin, and cutinase are not single enzymes but large genera of enzymes as there are many different sources of these enzymes each of which result in a structurally distinct enzyme which structural differences can result in functional differences among the different species and the specification provides evidence that for the instant reactions, even trypsin, (which clearly from Example 3 appeared to be the most active of the enzymes), exhibits variability in its successful use depending on the source of the enzyme. Such variability is even more likely for enzymes like pepsin which reacted very poorly with the one exemplified organic reactant or cutinase for which no successful reactions are disclosed. Similarly for claim 1, the claim still recites many enzymes as both trypsin and cutinase are large genera of enzymes, the specification clearly has shown no examples of successful reactions using any cutinase and only showed two sources of trypsin (i.e., bovine and porcine pancreas) which were successful. Furthermore, claim 1 recites an enormous genus of organic reactants for which the



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disclosed examples do not begin to cover the claimed scope yet even within the compounds tested in the specification, several were unsuccessful and thus there is clearly a high degree of unpredictability in successful use of other compounds.

Applicants have submitted a declaration of the inventors showing some additional successful examples using a cutinase with dimethyldimethoxysilane and trypsin with diethyldiethoxygermane. However, this data simply provides a few more examples of the unpredictability of the claimed scope as clearly the cutinase used in this example like pepsin and papain is a very poor catalyst which was successful only under some conditions (i.e., showed successful catalysis only at high enzyme levels for very long time periods) and does nothing to remedy the fact that the disclosed data does not begin to cover the full scope of the claims. Furthermore, the declaration reports post filing data and thus does nothing to show enablement of the scope of the instant claims at the time of filing of the instant application.

Applicants should note that claims 19 and 33-35 have not been included in the instant rejection as in each of the claims. either or both the scope of organic reactants and the scope of enzymes is limited sufficiently that one could randomly test

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those reactants/enzymes encompassed to determine which would be successful without undue experimentation.

Applicants argue that the specification does provide guidance for by providing reasons for the failure of particular compounds to react. However, these reasons do not appear to be consistent throughout the various examples such that one could use them to predict what compounds would be successful. Furthermore, even if these statements would have appeared to provide a consistent direction for selecting successful compounds, it is noted that all of claims 1, 5-10, and 12-14 still include enormous numbers of compounds which are very large and hydrophobic and thus would be expected to be unsuccessful. While enablement is not precluded by the presence of a few non-operative embodiments within the scope of the claims, the vast majority of the scope of the claimed organic reactants should not be expected to be unsuccessful, which would appear to be the case here as these claims are not limited to organic reactants with similar size and hydrophilicity/hydrophobicity to those which are successfully used. For all the reasons above the rejection is maintained.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 9, 10, 16, 19, 24, 25, 27-32 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Cha et al.

Cha et al. teach the formation of a polymerized silica product from tetraethoxysilane using an enzymatic hydrolysis and condensation with the proteases trypsin, papain or silacatein in aqueous buffer at neutral pHs and temperatures of 20°C. As such Cha et al. anticipate all of the instant claims.

Applicants argue that the previous statement by the examiner that "applicants argument that BSA is shown in the specification as being unable to catalyze the reaction as compared to the proteases is not persuasive as the reactions are not the same. A different substrate was used by Cha et al. than used by applicants and there is substantial evidence that not every protein can catalyze the reaction with every substrate." is an admission that Cha et al. does not anticipate as if the results of Cha et al. are not applicable to any substrate other than the one used by Cha et al. and the substrate of Cha et al. is different than that used by applicants then Cha et al. cannot anticipate. However this is incorrect. The examiner's statement referred to a comparison of Cha et al. results (using

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BSA and TEOS) with a specific experiment in applicants specification (Example 2 and 3). However, applicants claims are NOT limited to what was being discussed from the specification. Applicants claims DO encompass Cha et al.'s substrate (TEOS) and thus Cha et al. does anticipate the claims.

Applicants further argue that in Example 10 applicants investigated the condensation reaction of tetraethoxysilane with trypsin as a catalyst. In that Example, applicants found that in comparison to a control reaction, trypsin did not catalyze the polycondensation of tetraethoxysilane in an aqueous medium at pH 6.8. Specifically, trypsin did not hydrolyze or condense tetraethoxysilane during the three-hour reaction (page 34, paragraph 112) and the reaction of Cha et al. is even shorter. However, applicants also show in example 10 that given a longer reaction that trypsin did catalyze the polycondensation of TEOS. The claims do not recite any specific time period of reaction nor to the specify how much product must be formed. The results of Cha et al. clearly indicate that about twice as much product was formed with trypsin and papain present as was formed without any added protein. Furthermore, claims 16, 31, 32, and 34 specifically recite TEOS as one of the designated reactants which they state the specification shows is successful with trypsin. Applicants appear to be arguing that this compound is

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one of those shown to be successful in response to the enablement rejection while arguing that the same reaction is NOT successful in response to the 102 and thus does not anticipate their claims.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Friedrich (WO02/22842) in view of the 1997 Sigma catalog.

Friedrich teaches the formation of organic siloxanes from a variety of organic silanes using an enzymatic hydrolysis and condensation with a lipase in aqueous or organic solvents at neutral pHs and temperatures of about 25°C. The organic silanes

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used included phenyltriethoxysilane and tetrabutoxysilane.

Friedrich does not specifically teach using the lipases recited in the instant claims.

The 1997 Sigma catalog shows that the *Candida antarctica* lipase, *Rhizomucor miehei* lipase and wheat germ lipases are all well known commercially available lipases.

As Friedrich teaches the formation of organic siloxanes from a variety of organic silanes using an enzymatic hydrolysis and condensation with any lipase, it would have been obvious to one of ordinary skill in the art to select one of the commercially available lipases taught by the Sigma catalog as the lipase to use for the reaction disclosed by Friedrich as these are easily available and well characterized.

Applicants argue that Friedrich discloses that all lipases are suitable for the process of its invention and preferred lipases are from the *Pseudomonas* species but contrary to this teaching, Table 2 of the present application sets forth that *Pseudomonas cepacia* lipase and *Pseudomonas fluorescens* lipase, are unable to catalyze the hydrolysis and condensation of those organic reactants encompassed by applicants' claims. Thus, in spite of Friedrich et al.'s statement that any lipase is suitable for the polycondensation of organic silicon compounds, that is clearly not the case. As Friedrich give only guidance

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contrary to the teachings of applicants specification, one skilled in the art would not be led to select the specific lipases taught and claimed by applicant when given Friedrich and the Sigma catalog. Actually, more than likely, one skilled in the art would select lipases which Applicants have specifically described as inoperable. However, this is not persuasive as Friedrich is teaching the polycondensation of different organic reactants than those for which *Pseudomonas cepacia* lipase and *Pseudomonas fluorescens* lipase were shown by applicants to be unsuccessful. However applicants claims encompass these organic reactants. Furthermore, the rejection did not state that a skilled artisan would have found it obvious to use either the *Pseudomonas cepacia* lipase or *Pseudomonas fluorescens* lipase but that a skilled artisan would have found it obvious to use one of the commercially available lipases taught by the Sigma catalog which include several enzymes within the scope of applicants claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Prouty/  
Primary Examiner  
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